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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/596,083	05/30/2006	Dominique Jean-Pierre Mabire	PRD-2122USPCT	1664

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EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/596,083	MABIRE ET AL.	
	Examiner	Art Unit	
	EMILY BERNHARDT	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8 and 10-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4,16,24,25 and 28* is/are allowed.

6)☒ Claim(s) *1,6,8,12,13,17,20,23,29 and 30* is/are rejected.

7)☒ Claim(s) *2,3,10,11,14,15,18,19,21,22,26 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claims 8, 13,17,20,23 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claims 8,17,20 and 23 are of indeterminate scope for the following reasons. Defining a disease(s) by its (their) underlying cause renders the scope of intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or "associated with" PARP enzymes or in ways not yet understood. Additionally, determining whether a given disease responds or not to PARP inhibition involves much experimentation since a negative response from one patient does not mean the drug isnt useful as no drug has 100% effectiveness. Further exacerbating the scope is the fact that there are many types of PARP- at least 16 known to date which have not been fully investigated other than as research tools. Thus what "success rate" determines if a particular inhibitor is effective and how many patients (and dosage regimens) need to be tested? The test for determining compliance with 35 USC 112, par.two is whether applicants have clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires.

2. The routes recited in claim 13 should be indicated as alternate routes . An "or" could be added after each consecutive preparation so it clearly reflects applicants. intent.

3. The "product" recited in claim 29 requires clarification. The term is broad enough to include by-products of which there would be many given the many alternative routes and reagents recited.

Claim 30 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claim recites a "pharmaceutical composition" as the product made by claim 13. However only compounds of claim 1 are made in claim 13.

Claims 8,17,20 and 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of uses covered by the method claims are not enabled except for those uses recited in claims 10,11,18,19,21,22,24 and 25. The notion that PARP inhibitors have such a range of uses as those described in the specification (on pp.2-4) is not substantiated by the current state of the art. Li cited by applicants as an example of the state of the art, evidences that research in this area is very preliminary. See concluding remarks regarding the unpredictability of success in humans since "the function of PARP1 and other members of PARP family have yet to be firmly established". References such as Lord, Zhang and Larner, newly provided by the examiner while discussing potential use for treating cancers, ischaemia, inflammation and neurodegenerative diseases, do not evidence that such compounds as a class are known to treat all types of cancers, all types of ischaemias, inflammatory disorders, neurodegenerative diseases. In Lord the discussion on cancers that may be treated are

currently limited to a specific type, i.e those that are BRCA1 and BRCA2 deficient with a few PARP inhibitors in clinical trials that is ongoing as of 2008, considerably later than applicants' filing date. In Zhang it is stated on p.216, section 6: "Almost all PARP inhibitors are only at the research or early development stage, except for nicotinamide, a B-family vitamin, which is undergoing clinical trials for Type I diabetes with PARP inhibition as possible mechanism." Larner directed to a discussion of neuronal cell death is even less convincing of any known therapeutic efficacy. In the abstract, last sentence is stated: "The place of PARP inhibitors as a clinical therapy to prevent neuronal cell death remains to be determined." Concluding remarks on p.485, last paragraph to top of p.486 in the article cautions that reliance on animal models is at least needed. Note also the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a),August 2000 edition which considers factors such as:

1) Breadth of the claims- The claims cover (but are not limited to) to all types of all cancers, inflammatory and neurodegenerative diseases, as well as HIV of which there are many arising from many different and unknown etiology such as Huntington's Disease, alcoholism, Pick's Disease, ALS, prion diseases and many others for which therapy is very limited or unknown- this just for one class of disorders;

2) Level of skill in this art- there are no drugs known to have such a spectrum of clinical applications much less having the activity relied on herein and thus the level of skill is low ;

3) State of the prior art- no compounds similar in structure have demonstrated such a range of uses in preclinical much less clinical trials;

4) Working examples- There are no test(s) directed to the many uses pointed out above which are art-recognized for predicting *in vivo* efficacy;

Thus in view of the above the rejection is being applied.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,6,8,13,29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Mabire (WO'837). The commonly assigned publication describes several compounds within the claims' scope for uses including those embraced herein. See for example on p.78, egs. 146 and 148 and on p.80. no.50. These compounds were prepared by routes B4 and B7. B4 corresponds to the 1st process recited in claim 13.

Uses taught by Mabire include CNS disorders such as Alzheimer's, Parkinson's Disease, Huntington's Disease, ischemic injuries, etc. all embraced herein.

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Freyne (EP'564). Freyne describes compounds including one within the instant scope for uses including cancer. See example 126-c on p.80 and uses described on p.31. While main claim 1 excludes the species in Freyne, claim 8 does not.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1,6,13,29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freyne. The teachings of Freyne discussed in the above 102 rejection is incorporated herein. While the species in Freyne (no. 126-c) is excluded by proviso in the claims rejected herein, the subject matter still embraced is obvious for more than one reason. Closest compounds to 126-c are simply higher homologs at the 3-position or are substituted with other azoles included within the definition of "Z" herein. However, note that Freyne teaches higher alkyls can be present at the 3-position. See definition of R27 on p.3 and that azoles other than imidazole can be present on the methylene group directly attached to the benzo portion of the quinoxaline ring. See definition of X1-X2 which includes triazoles of formula (c-4). Claim 13 is also rejected since Freyne employs the same process as route b) herein to make imidazole species, 126-c. Thus it would have been obvious to one skilled in the art at the time the instant invention was made to modify the closest species in Freyne (126-c) by inserting higher alkys at the 3-position and/or replacing the imidazole ring with triazoles with expectation that such resulting compounds will also have the uses reported in Freyne in view of the equivalency teachings outlined above.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Freyne as applied to claims 1,6,13,29 and 30 above, and further in view of Zhi (US'505). While Freyne contemplates the addition of co-ingredients that are useful for various intended uses (see p.32), particular mention of adding chemotherapeutic agents is not described. However, Zhi is applied to show that compounds having the same type of activity as

Freyne are conventionally mixed with other active ingredients including chemotherapeutic agents. See p.9 section [0140] in Zhi. Thus it would have been obvious to one skilled in the art at the time the instant invention was made to combine compounds such as 126-c in Freyne included within the instant scope with known anticancer agents as an obvious expedient in the preparation of therapeutic compositions in view of the teachings outlined in Zhi.

Claims 2,3,10,11,14,15,18,19,21,22,26,27 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 4,16,24,25 and 28 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is 571-272-0664.

If attempts to reach the examiner by telephone are unsuccessful, the acting supervisor for AU 1624, James O. Wilson can be reached at 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Emily Bernhardt/
Primary Examiner, Art Unit 1624